Notice of Allowability	Application No.	Applicant(s)	
	09/578,507	RAMASUBRAMANYAN, NATARAJAN	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed on 10/5/04*.

2. ☒ The allowed claim(s) is/are *1-11,13-19,21-29,50,51,54 and 56-84*.

3. ☒ The drawings filed on *26 May 2000* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *1104* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Applicant's representative B.J. Sadoff on 12/2/04.

The application has been amended as follows:

1. (Currently Amended) A method for purifying plasmid DNA from a mixture ~~of same~~ containing plasmid DNA and at least one host cell impurity comprising the following steps:

(a) forming a solution comprising a salt with said mixture wherein said solution has a salt concentration in the range of about 2M to 4M to allow selective binding of said at least one host cell impurity to a chromatography support comprising a hydrophobic pendent group ~~hydrophobic interaction media~~;

(b) contacting said solution containing plasmid DNA with said support at a salt concentration whereby ~~hydrophobic interaction media under conditions that~~ said at least one impurity binds to said hydrophobic pendent group ~~the hydrophobic interaction media~~ to form a complex; and

(c) collecting unbound plasmid DNA from said complex without further chromatographic separation;

wherein said method is conducted in the absence of organic solvents, detergents, glycols, hexamine cobalt, spermidine, and polyvinylpyrollidone.

2. (Original) The method of claim 1 wherein the at least one impurity is selected from the group consisting of RNA, endotoxin, chromosomal DNA and protein.

3. (Original) The method for claim 1 wherein the at least one impurity is an endotoxin.

4. (Original) The method of claim 1 wherein the salt comprises an anion or cation selected from the group consisting of acetate, phosphate, carbonate, SO_4^{2-}, Cl^-, Br^-, NO_3^-, Mg^{2+}, Li^+, Na^+, K^+ and NH_4^+.

5. (Previously Presented) The method of claim 4 wherein the salt is ammonium sulfate.

6. (Original) The method of claim 5 wherein ammonium sulfate is present at a concentration of about 2M.

7. (Previously Presented) The method of claim 1 wherein the solution comprises sodium salts in a concentration range of about 2M to 4M.

8. (Original) The method of claim 7 wherein the sodium salt is sodium chloride.

9. (Original) The method of claim 8 wherein the sodium salt is sodium chloride in a concentration of about 2M.

10. (Original) The method of claim 1 wherein the pH of the solution has a range of about 6.8 to about 7.4.

11. (Original) The method of claim 1 wherein the pH of the solution is about 7.4.

Claim 12. (Canceled)

13. (Currently Amended) The method of claim ~~12~~ 1 wherein said pendent groups are selected from the group consisting of C_3 to C_{10} alkyl groups and mixtures thereof.

14. (Currently Amended) The method of claim ~~12~~ 1 wherein the ~~hydrophobic interaction media are~~ support is selected from at least one of ~~the group consisting of~~ a methacrylate polymer and a ~~or~~ copolymer backbone and said pendent group is at least one of ~~bound to a least one of~~ a propyl, butyl, hexyl, octyl, nonyl, ~~or~~ decyl or phenyl group~~ligand~~.

15. (Currently Amended) The method of claim 1 ~~12~~ wherein the support ~~media~~ is at least one of a methyacrylate ethylene glycol copolymer backbone or a cross-linked agarose backbone.

16. (Currently Amended) The method of claim 1 ~~12~~ wherein the support is in the form of bead in the size range of 15 to 100 μm.

17. (Currently Amended) A method of separating supercoiled plasmid DNA from a mixture of supercoiled plasmid DNA and relaxed plasmid DNA and, optionally, at least one host cell impurity comprising the following steps:

(a) forming a solution by adding a salt to the mixture of supercoiled plasmid DNA and relaxed plasmid DNA and, when present, said at least one host cell impurity;

(b) contacting the solution with a chromatography support comprising a hydrophobic pendent group at a first salt concentration ~~hydrophobic interaction media under a first condition~~ where both the supercoiled plasmid DNA and relaxed plasmid DNA bind to the hydrophobic pendent group ~~interaction media~~ to form a bound first mixture;

(c) altering the first salt concentration ~~condition~~ surrounding the bound first mixture to a second salt concentration ~~condition~~ to remove relaxed plasmid DNA from the bound first mixture to form separate components containing a second bound mixture and relaxed plasmid DNA; and

(d) modifying the second salt concentration ~~condition~~ surrounding the said second bound mixture to a third salt concentration ~~condition~~ to remove supercoiled plasmid DNA from said second bound mixture ~~to form separate components containing hydrophobic interaction media and supercoiled plasmid DNA~~.

18. (Original) The method of claim 17 wherein the at least one host cell impurity is selected from the group consisting of RNA, endotoxin, chromosomal DNA and protein.

19. (Original) The method for claim 17 wherein the at least one host cell impurity is an endotoxin.

Claim 20. (Canceled)

21. (Currently Amended) The method of claim 17 ~~20~~ wherein said pendent groups are selected from the group consisting of C_3 to C_{10} alkyl groups.

22. (Currently Amended) The method of claim 17 ~~20~~ wherein the ~~hydrophobic interaction media~~ support is selected from ~~the group consisting~~ at least one of a methacrylate polymer ~~or~~ and a copolymer backbone ~~bound to a least one of~~ and said pendent group is at least one of a propyl, butyl, hexyl, octyl, nonyl, decyl or phenyl group ~~or a mixture of these as ligands~~.

23. (Currently Amended) The method of claim ~~20~~ 17 wherein the ~~media~~ support is at least one of a methyacrylate ethylene glycol copolymer backbone or a cross-linked agarose.

24. (Currently Amended) A method of claim ~~20~~ 17 wherein the ~~media~~ support is a resin in the form of beads in the size range of 15 to 100 μm.

25. (Original) The method of claim 17 wherein the salt comprises an anion or cation selected from the group consisting of acetate, phosphate, carbonate, SO_4^{2-}, Cl^-, Br^-, NO_3^-, Mg^{2+}, Li^+, Na^+, K^+ and NH_4^+.

26. (Currently Amended) The method of claim 25 wherein the salt is ammonium sulfate and said first salt concentration is in the range of ~~in a concentration range of~~ 2.5M to 4M.

27. (Currently Amended) The method of claim 17 wherein the first ~~condition~~ mixture comprises ~~equilbrating~~ said ~~media~~ support equilibrated with a salt solution containing ammonium sulfate which is present in a concentration range of about 2.5M to 4M.

28. (Currently Amended) The method of claim 17 wherein ~~the second condition~~ said altering comprises washing the ~~media~~ support with a salt solution containing ammonium sulfate in a concentration of about 2.35M to about 2.45M.

29. (Currently Amended) The method of claim 17 wherein the ~~said third condition~~ modifying comprises washing said second bound mixture with a salt solution containing ammonium sulfate in a concentration of about 1M to 2.3M.

Claims 30-49. (Canceled)

50. (Currently Amended) The method of ~~any one of claims 17 and 41~~ claim 17 wherein said altering and said modifying are combined in a continuous process comprising gradient elution of said relaxed plasmid DNA and supercoiled plasmid DNA ~~by mixing said bound first mixture with an ammonium sulfate containing salt solution with a continuously varying~~

~~concentration of ammonium sulfate, said concentration varying from about 3M to about 1 M ammonium sulfate, and said relaxed plasmid DNA is collected in a first eluted volume and said supercoiled plasmid DNA is collected in a second eluted volume~~.

51. (Currently Amended) The method of claim ~~41~~ 17 wherein said separate relaxed plasmid DNA component and said separate supercoiled plasmid DNA are collected and isolated.

Claims 52 and 53. (Canceled)

54. (Currently Amended) A method of enriching supercoiled DNA relative to relaxed DNA in a mixture thereof, the method comprising :

(a) forming a first solution by adding a salt to the mixture of supercoiled DNA and relaxed DNA;

(b) contacting the first solution with a ~~hydrophobic interaction media under a first condition~~ chromatography support comprising a hydrophobic pendent group at a first salt concentration where both the supercoiled DNA and relaxed DNA bind to the ~~hydrophobic interaction media~~ pendent group to form a bound first mixture;

(c) altering the first ~~condition~~ salt concentration surrounding the bound first mixture to a second ~~condition~~ salt concentration to remove relaxed DNA from the bound first mixture to form separate components containing a second bound mixture and relaxed DNA; and

(d) modifying the second ~~condition~~ salt concentration surrounding the said second bound mixture to a third ~~condition~~ salt concentration to remove supercoiled DNA from said second

bound mixture to form separate components containing ~~hydrophobic interaction media~~ the support and supercoiled DNA.

Claim 55. (Canceled)

56. (Currently Amended) The method of claim ~~55~~ 54 wherein said pendent groups are selected from the group consisting of C_3 to C_{10} alkyl groups.

57. (Currently Amended) The method of claim ~~55~~ 54 wherein the ~~hydrophobic interaction media~~ support is selected from ~~the group consisting~~ at least one of a methacrylate polymer and a ~~or~~ copolymer backbone and said pendent group is at least one of ~~bound to a least one of~~ a propyl, butyl, hexyl, octyl, nonyl, ~~or~~ decyl or phenyl group ~~a mixture of these as ligands~~.

58. (Currently Amended) The method of claim ~~55~~ 54 wherein the support ~~media~~ is at least one of a methyacrylate ethylene glycol copolymer backbone or a cross-linked agarose.

59. (Currently Amended) A method of claim ~~55~~ 54 wherein the support ~~media~~ is a resin in the form of beads in the size range of 15 to 100 μm.

60. (Previously Presented) The method of claim 54 wherein the salt comprises an anion or cation selected from the group consisting of acetate, phosphate, carbonate, SO_4^{2-}, Cl^-, Br^-, NO_3^-, Mg^{2+}, Li^+, Na^+, K^+ and NH_4^+.

61. (Currently Amended) The method of claim 60 wherein the first solution ~~salt~~ is ammonium sulfate in a concentration range of 2.5M to 4M.

62. (Currently Amended) The method of claim 54 wherein the first ~~condition~~ mixture comprises ~~equilbrating~~ said support equilibrated ~~media~~ with a salt solution containing ammonium sulfate which is present in a concentration range of about 2.5M to 4M.

63. (Currently Amended) The method of claim 54 wherein said altering ~~the second condition~~ comprises washing the support ~~media~~ with a salt solution containing ammonium sulfate in a concentration of about 2.35M to about 2.45M.

64. (Currently Amended) The method of claim 54 wherein the said modifying ~~third condition~~ comprises washing said second bound mixture with a salt solution containing ammonium sulfate in a concentration of about 1M to 2.3M.

65. (New) A method for purifying plasmid DNA from a mixture of same containing plasmid DNA and at least one host cell impurity comprising the following steps:

(a) forming a first solution comprising a first salt with said mixture wherein said first solution has a salt concentration in the range of about 2M to 4M to allow selective binding of said at least one host cell impurity to a chromatography support comprising a hydrophobic pendent group;

(b) contacting said first solution containing plasmid DNA with said support at a first salt concentration whereby said at least one impurity binds to said hydrophobic pendent group to form a complex;

(c) separating unbound plasma DNA from said complex;

(d) forming a second solution comprising a second salt comprising said unbound plasmid DNA with a second salt concentration, wherein said second salt concentration is different from said first salt concentration;

(e) contacting said second solution with a chromatography support comprising a hydrophobic pendent group wherein said unbound plasmid DNA binds to said hydrophobic pendent group; and

(f) collecting supercoiled DNA from said chromatography support of step (e) by altering the salt concentration of said chromatography support of step (e).

66. (New) The method of claim 65 wherein the at least one impurity is selected from the group consisting of RNA, endotoxin, chromosomal DNA and protein.

67. (New) The method for claim 65 wherein the at least one impurity is an endotoxin.

68. (New) The method of claim 65 wherein at least one of the first salt and the second salt comprises an anion or cation selected from the group consisting of acetate, phosphate, carbonate, SO_4^{2-}, Cl^-, Br^-, NO_3^-, Mg^{2+}, Li^+, Na^+, K^+ and NH_4^+.

69. (New) The method of claim 68 wherein at least one of the first salt and the second salt is ammonium sulfate.

70. (New) The method of claim 69 wherein ammonium sulfate is present at a concentration of about 2M.

71. (New) The method of claim 65 wherein at least one of the first solution and the second solution comprises sodium salts in a concentration range of about 2M to 4M.

72. (New) The method of claim 71 wherein the sodium salt is sodium chloride.

73. (New) The method of claim 72 wherein the sodium salt is sodium chloride in a concentration of about 2M.

74. (New) The method of claim 65 wherein the pH of at least one of the first solution and the second solution has a range of about 6.8 to about 7.4.

75. (New) The method of claim 65 wherein the pH of at least one of the first solution and the second solution is about 7.4.

76. (New) The method of claim 65 wherein said pendent groups are selected from the group consisting of C_3 to C_{10} alkyl groups and mixtures thereof.

77. (New) The method of claim 65 wherein the support is selected from at least one of a methacrylate polymer and a copolymer backbone and said pendent group is at least one of a propyl, butyl, hexyl, octyl, nonyl, decyl or phenyl group.

78. (New) The method of claim 65 wherein the support is at least one of a methyacrylate ethylene glycol copolymer backbone or a cross-linked agarose backbone.

79. (New) The method of claim 65 wherein the support is in the form of bead in the size range of 15 to 100 μm.

80. (New) The method of claim 50 wherein said continuous process further comprises contacting said first bound mixture with an ammonium sulfate containing salt solution with a continuously varying concentration of ammonium sulfate, said varying concentration ranging

from about 3M to about 1M ammonium sulfate, whereby said relaxed plasmid DNA is collected in a first eluted volume and said supercoiled DNA is collected in a second eluted volume.

81. (New) The method of claim 17 further comprising separating said at least one host cell impurity from said supercoiled plasmid DNA and said relaxed plasmid DNA on a separate chromatography support prior to said contacting.

82. (New) The method of claim 81 wherein said separate chromatography support comprises a hydrophobic pendent group.

83. (New) The method of claim 82 wherein said separating comprises chromatographic separation of said at least one host cell impurity at a salt concentration less than said first salt concentration, whereby said at least one host cell impurity binds to said hydrophobic pendent group of said separate chromatography support.

84. (New) The method of claim 54 wherein said altering and said modifying are combined in a continuous process comprising gradient elution of said relaxed plasmid DNA and supercoiled plasmid DNA.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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